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(54) ANTIBACTERIAL PHARMACEUTICAL AND FEEDSTUFF COMPOSITIONS

(71) We, ASTRA—EWOS AB, a Swedish Body Corporate, of Fack, S—151 20 Sodertalje, Sweden, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to a new antibacterial system, to compositions containing it, particularly to foodstuff and animal feedtsuff compositions containing it, to the use of such antibacterial systems, to the preparation of such foodstuffs and animal feedstuffs and to their use in meat production.

The present invention is concerned with foodstuffs and animal feedstuffs comprising an antibacterial system, which system exerts an antibacterial effect in the gastrointestinal tract.

It is previously known that domestic animal live stocks, especially young animals, are subjected to severe gastrointestinal infections which mainly depend on infections of *E. coli* and different species of *Salmonella*. Hitherto know methods to eliminate these infections include thereby either the administration of a therapeutical amount of antibiotics with the risk for the formation of antibiotic resistact bacterial species attached thereto, or to carry out a vaccination of the live stocks, which leads to high costs as vaccines and vaccinations are relatively expensive. Another chemotherapeutically active agent used is i.a. trimethoprimsulpha.

It has now surprisingly been found possible to avoid these drawbacks, and to prevent and/or eliminate such bacterial infections by means of the present invention, which provides a foodstuff or animal feedstuff comprising an antibacterial system which is activated in the gastrointestinal tract, and comprises a lactoperoxidase, a thiocyanate and a solid, water soluble peroxide donor which is an alkali metal percarbonate, an alkaline earth metal peroxide, or a carbamide peroxide.

In addition to the antibacterial system, the foodstuff or animal feedstuff suitably contains nutritional elements known *per se*.

According to a preferred embodiment, the feedstuff comprises a thiocyanate in an amount of at least 16 ppm of the foodstuff calculated as NaSCN, the solid water-soluble peroxide donor in an amount of at least 21 ppm of the foodstuff calculated as sodium percarbonate (where the peroxide donor is not sodium percarbonate, its amount is calculated in conventional manner as the amount of sodium percarbonate which would give rise to the same amount of H_2O_2), and a lactoperoxidase, in an amount of at least 1 mg/kg foodstuff, the lactoperoxidase being in purified form and/or in the form of a lactoperoxidase-containing milk product, and the molar ratio of peroxide donor to thiocyanate being less than 4:1, preferably 1:1 to 2:1.

According to a further preferred embodiment, the feedstuff comprises a thiocyanate in an amount of 160 to 3500, preferably 160 to 1750 ppm/kg foodstuff calculated as NaSCN, a peroxide donor in an amount of 210 to 4000, preferably 210 to 2000, ppm/kg foodstuff calculated as Na-percarbonate, and a lactoperoxidase in an amount of 10 to 200, preferably 10 to 100, mg/kg.

The water-soluble peroxide donor is preferably sodium percarbonate, and suitably has been coated with a protecting layer which is soluble in the intestinal tract, and which layer preferably consists of cellulose acetatephthalate.

The present invention also provides a process for the preparation of a foodstuff or animal feedstuff wherein an antibacterial system which is activated in the gastrointestinal tract is added to a foodstuff or animal feedstuff known *per se*, said system comprising a lactoperoxidase, a thiocyanate, and a solid, water-soluble peroxide donor

which is an alkali metal percarbonate, alkaline earth metal peroxide, or a carbamide peroxide.

According to a further embodiment of the present invention, there is provided a process for more efficient meat production, whereby meat producing animals, e.g. calves and pigs are fed with a feedstuff of the present invention.

According to a still further embodiment of the present invention there is provided the antibacterial system which comprises a lactoperoxidase, a thiocyanate, and a solid, water-soluble peroxide donor selected, which is an alkali metal percarbonate, an alkaline earth metal peroxide or a carbamide peroxide and also a pharmaceutical composition comprising this antibacterial system together with a pharmaceutically acceptable carrier.

A further embodiment of the present invention is a method for treating gastrointestinal infections in mammals, excluding humans, suffering from gastrointestinal infections caused by bacteria, whereby a therapeutically effective amount of the antibacterial system given above is administered orally.

Animals treated are normally pigs, calves and poultry, and fur-producing animals such as minks and foxes. Pets such as cats and dogs may also be treated.

The thiocyanate is preferably administered to the animal in an amount such that the concentration thereof in the intestinal tract is at least 0.1, preferably 0.2 to 0.4 mM, or in certain cases, 0.5 to 1.0 mM may be useful but the concentration should not exceed toxical concentrations (10 mM). The peroxide donor is preferably administered such that the amounts of thiocyanate and of H_2O_2 are equimolar i.e. that the concentration of H_2O_2 formed is at least 0.1, preferably 0.2 to 0.4 mM. However, the concentration of H_2O_2 may be higher than that of the thiocyanate but should suitably be less than 4 times the concentration of the thiocyanate. The amount of lactoperoxidase administered is dependent on the activity of the enzyme but based on the assumption that 1 mg contains 50 units (U), at least 1 mg of enzyme should preferably be present per litre of digestive juice.

Therefore, preferably in the intestinal tract, the concentration of thiocyanate is at least 0.1 mM, preferably 0.2 to 0.4 mM, the concentration of peroxide donor is such that the concentration of H_2O_2 is 0.1 mM, preferably 0.2 to 0.4 mM, and the concentration of lactoperoxidase is 1 mg/l (50 U/l). The latter may be varied but should normally be 1 to 2 mg/l (50 to 100 U/l).

1 unit of lactoperoxidase is the amount of lactoperoxidase which forms 1 mg of pyrogalline from pyrogallol in 20 sec. at pH 6.0 and 20°C.

The amount of lactoperoxidase in bovine whey (unpasteurized) or in ultrafiltrated whey may of course vary. Bovine milk contains, according to the literature, lactoperoxidase in an amount of about 30 mg/l, whereby the amount of lactoperoxidase in human milk, according to the literature, is about 1/30 of that in bovine milk. Lactoperoxidase is also found in other bovine milk products as skim milk powder, which may be used as well.

Salts of thiocyanate used are preferably sodium, potassium, and ammonium salts.

LD_{50} of thiocyanate is 484 mg/kg bodyweight when injected intravenously in mice and 764 mg/kg bodyweight when administered orally to rat.

In clinical use, the antibacterial systems of the invention is administered normally orally, or rectally in the form of a pharmaceutical preparation, which also contains a pharmaceutically acceptable carrier. The carrier may be a solid, semisolid or liquid diluent or a capsule. Usually the amount of active ingredients is 0.1 to 99% by weight of the preparation, suitably 2 to 50% by weight in preparation for oral administration.

The antibacterial system of the present invention, apart from being activated in the gastrointestinal tract, is also active in topical applications and thus the present invention further provides a method for treating topical bacterial infections in mammals excluding humans which comprises administering topically to a mammal suffering from topical bacterial infection an antibacterial system or pharmaceutical preparation of the present invention.

In the preparation of pharmaceutical preparations containing an antibacterial system of the present invention in the form of dosage units for oral administration, the ingredients may be mixed with a solid, pulverulent carrier, such as lactose, saccharose, sorbitol, mannitol, starch such as potato starch, corn starch or amylopectin, cellulose derivatives or gelatins, as well as with an anti-friction agent such as magnesium stearate, calcium stearate or polyethyleneglycol waxes, and be pressed into tablets. If coated tablets are wanted, the above-prepared core may be coated with a solution of a polymer which dissolves or is permeable in the intestinal tract. To this coating a dye may be added in order to easily distinguish between tablets with different active compounds or with different amounts of the active compound present.

In the preparation of soft gelatine capsules (pearl-shaped, closed capsules), which consist of gelatine and e.g. glycerine, or in the preparation of similar closed capsules, the active compound is mixed with a vegetable oil. Hard gelatine capsules may contain granules of the active compound mixed with a solid, pulverulent carrier such as lactose, saccharose, sorbitol, mannitol, starch (e.g. potato starch, corn starch or amylopectin),

cellulose derivatives or gelatine.

Dosage units for rectal administration may be prepared in the form of suppositories, which contain the active substance in a mixture with a neutral fat base, or they may be prepared in the form of gelatine-rectal capsules which contain the active substance in a mixture with a vegetable oil or paraffin oil.

Liquid preparations for oral administration may be in the form of syrups or suspensions, e.g. solutions containing from 0.2% by weight to 20% by weight of the active substances described, whereby the residue consists of sugar and a mixture of ethanol, water, glycerol and propylene glycol. If desired, such liquid preparations may contain colouring agents, flavouring agents, saccharine and carboxymethylcellulose as a thickening agent. The peroxide donor is thereby present in form of microencapsulated particles.

The preparation of pharmaceutically tablets for peroral use is suitably carried out in accordance with the following method.

The solid substances are ground or sieved to a certain particle size. The binding agent is homogenized and suspended in a certain amount of solvent. The therapeutic compound and necessary auxiliary agents are mixed by continuous and constant mixing with the binding agent solution, which may consist of a polymer which dissolves or is permeable in the intestinal juices, and are moistened so that the solution is uniformly distributed without overmoistening any parts. The amount of solvent is usually so adapted that the mass achieves the consistency of wet snow. The moistening of the pulverulent mixture with the binding agent solution causes the particles to gather together slightly into aggregates and the real granulating process is carried out in such a way that the mass is pressed through a sieve in the form of a net of stainless steel having a mesh size of about 1 mm. The mass is then placed in thin layers on a tray to be dried in a drying cabinet. This drying takes place during 10 hours and has to be standardized carefully as the degree of dampness of the granulate is of utmost importance for further processing and for the properties of the tablets. Drying in a fluid bad may possibly be used. In this case the mass is not put on a tray but is poured into a container having a net bottom.

After the drying step the granules are sieved so that the required particle size is obtained. Under certain circumstances powder has to be removed.

To the so-called final mixture, distintegrating, antifriction agents and antiadhesive agents are added. After this mixture the mass shall have its right composition for the tabletting step.

The cleaned tablet punching machine is provided with a certain set of punches and dies, whercupon the suitable adjustment for the weight of the tablets and the degree of compression is tested out. The weight of the tables is decisive for the size of the dose in each tablet and is calculated from the amount of therapeutic agent in the granules. The degree of compression affects the size of the tablet, its strength and its ability of disintegrate in water. Especially as regards the two latter properties the choice of compression pressure (0.5 to 5 ton) must be correctly balanced. When the right adjustment is set, the preparation of tablets is started and may be carried out at a rate of 20,000 to 200,000 tablets per hour. The pressing of the tablets requires different times and depends on the size of the batch.

The tablets are preferably coated with a coating e.g. with a layer of a polymer dissolvable or permeable in the intestinal tract.

The tablets are usually packed by machines having an electronic counting device. Suitable types of packages are glass and plastic gallipots, and also boxes, tubes and specific dosage adapted packages.

The daily dose of the active substance varies and depends on the type of administration and bacterial infection, but as a general rule it is 8 to 400 mg/day of sodiumthiocyanate and 10 to 500 mg/day of sodiumpercarbonate at peroral administration.

Pharmaceutical preparations containing an antibacterial system according to the invention are intended to be used in the treatment of bacterial infections in the gastorintestinal tract caused e.g. by *Shigella, Salmonella, E. coli, Vibrio colera, Pseudomonas (Ps. pyocyanea), Staphylococcus (Staph. albus, aureus), Streptococcus (Strep. viridans, Strep. faecalis, β-Streptococcus), Proteus.*

The present invention will be described in more detail in the following with reference to the Examples below.

Example 1.

A milk substitute was prepared from the following ingredients:

2 kg	of	ultrafiltrated wheypowder (500 mg of lactoperoxidase/kg)
66 kg	of	wheypowder
8 kg	of	fat
20 kg	of	animal protein
4 kg	of	vitamins, minerals
100 kg		

and

21 g	of	sodium percarbonate
16 g	of	sodium thiocyanate.

The ingredients were thoroughly mixed in a mixer. At the use thereof water is added to the dry mixture until a 10% aqueous solution is obtained (10% dry mixture). Such a milk substitute solution is normaly adminis-

tered in an amount of 4 litres per day per calf (=400 g of dry product per day).

The amount of sodium percarbonate may be varied in such a milk replacer from 210 to 420 ppm and the amount of thiocyanate from 160 to 320 ppm, whereby Na-percarbonate:NaSCN = 21:16.

Example 2.

A feedstuff additive for piglets was prepared from the following ingredients:

66.0 kg of feedstuff flour (steamtreated oats)
10.0 kg of iron salts (Fe^{2+}-salts)
3.5 kg of vitamins (vit. A, D, E, and C)
0.5 kg of trace elements (Cu, Co, I, Mn, Zn)
20.0 kg of ultrafiltrated wheypowder (500 mg of LP/kg)

100.0 kg

and

210 g of sodium percarbonate
160 g of sodium thiocyanate

The ingredients were thoroughly mixed in a mixer. The feedstuff is administered in dry form directly on the floor to the pigs from the age of 2 days to the age of 28 days. The daily dose of such a feedstuff is about 5 g per piglet, whereby the amount at each feeding occasion is about 0.5 g/piglet. The amount of sodium percarbonate may be varied in such a feedstuff from 2100 to 4200 ppm and the amount of sodium thiocyanate from 1600 to 3200 ppm, whereby the relation Na-percarbonate:NaSCN = 21:16.

Example 3.

A feedstuff for piglets was prepared from the following ingredients. The feedstuff is intended to be used when no sow milk is at hand or when very early weaning is considered.

60.0 kg of skim milk powder
3.5 kg of ultrafiltrated whey powder (500 mg of LP/kg)
15.0 kg of corn (ground, streamtreated oats and/or barley)
5.0 kg of fat
3.0 kg of hydrolyzed corn starch
2.5 kg of raw sugar
6.0 kg of glucose
5.0 kg of vitamins and minerals

100.0 kg

and

35 g of sodium percarbonate
27 g of sodium thiocyanate

The ingredients were thoroughly mixed in a mixer. The feedstuff is administered in dry form to the pigs whereby the feedstuff is given *ad libitum*. The daily intake is 30 to 200 g depending on the age of the piglet.

The amount of sodium percarbonate may be varied from 350 to 700 ppm, and the amount of NaSCN from 270 to 540 ppm, Na-percarbonate:NaSCN being 21:16.

Example 4.

A vitaminized mineral feedstuff for swine, as mother sows, was prepared from the following ingredients.

33.0 kg of calcium salt
35.0 kg of calcium / phosphorous salt ($CaHPO_4 . 2H_2O$)
13.0 kg of sodium chloride
0.4 kg of B-vitamin mixture
0.4 kg of vitamins A, C, D, and E
1.2 kg of trace element mixture (Fe, Zn, Mn, Cu, I)
17.0 kg of ultrafiltrated whey powder (500 mg of LP/kg)

100.0 kg

and

174 g of sodium percarbonate
135 g of sodium thiocyanate

The ingredients of the mineral feedstuff were thoroughly mixed and are diluted with corn and protein sources known and used *per se*. 3% of the vitaminized mineral feedstuff are used in the end mixture. Alternatively the vitaminized mineral feedstuff may be administered in amount of 30 to 150 g per animal per day directly into the trough without incorporation. The amount of sodium percarbonate may be varied from 1740 to 3480 ppm, and the amount of NaSCN from 1350 to 2700 ppm, Na-percarbonate:NaSCN being 21:16.

Example 5.

An electrolyte mixture was prepared from the following ingredients:

1.0 kg of potassium chloride
20.0 kg of sodium chloride
15.0 kg of sodium bicarbonate
64.0 kg of glucose

100.0 kg

and

97 g of sodium percarbonate
75 g of sodium thiocyanate
5 g of lactoperoxidase (50 U/mg)

The electrolyte mixture throughly mixed is used as follows: 25 g thereof is dissolved in 1 litre of water and is administered to pig or calf in an amount of about 10% of the bodyweight daily at established dehydration, or in order to prevent dehydration.

The amount of sodium percarbonate may be varied from 970 to 1940 ppm, and the

amount of sodium thiocyanate from 750 to 1500 ppm, the amount of Na-percarbonate: the amount of NaSCN being 21:16.

Example 6.

A gruel intended for small children was prepared from the following ingredients.

50.5 kg	of desalinated wheypowder
19.0 kg	of skim milk powder (⩾100 mg LP/kg)
14.0 kg	of fat mixture
8.0 kg	of lactose
7.5 kg	of steamtreated rice flour
1.0 kg	of vitamins and minerals
100.0 kg	

and

21 g	sodium percarbonate
16 g	sodium thiocyanate

The ingredients were thoroughly mixed in a mixer. The dry gruel mixture is dissolved in water having a temperature of 30 to 35°C as a 10 to 15% aqueous solution (10 to 15% dry matter) and is given in an amount of about 0.2 litres 4 to 5 times a day.

The amount of sodium percarbonate may be varied in such a gruel from 210 to 420 ppm and the amount of sodium thiocyanate from 160 to 320, whereby the amounts are preferably equimolar.

The sodium percarbonate used in Examples 1 to 6 above has been protected against too early reaction by coating a granulate thereof with a layer of polymer which dissolves or is permeable in the intestinal tract at first.

Such protecting polymers are waxes, cellulose acetate phthalate, and simiuar polymers which dissolve or are permeable in the intestinal tract. Further, a double coating may be used if a suspension before administration should give an alkaline environment.

Pharmaceutical preparations were prepared in accordance with the following Examples.

Example 7.

Sodium percarbonate granules containing 10% of active oxygen	100 g
Sodium thiocyanate	40 g
Lactoperoxidase (50 U/mg)	2 g
Polyvinylpyrrolidone	10 g
Lactose	50 g
Magnesium stearate	10 g

The lactoperoxidase was mixed with lactose and was granulated using a solution of polyvinylpyrrolidone.

Sodium percarbonate was mixed with sodium thiocyanate and the lactoperoxidase granules. Magnesium stearate was added, whereupon the granular mixture was tabletted.

The tablets obtained having an average weight of 212 mg were coated with a gastric juice resistant layer consisting of "Eudragit" [Registered Trade Mark].

Example 8.

Magnesium peroxide	50 g
Sodium thiocyanate	0.8 g
Lactoperoxidase (50 U/mg)	0.04 g
Polyvinylpyrrolidone	5 g
Lactose	100 g
Magnesium stearate	2 g

The three active components are granulated *per se* using polyvinylpyrrolidone as granulating agent. Lactose and magnesium stearate are added, whereupon the mixture is tabletted. The tablets obtained (1000 pieces) having an average weight of about 155 mg are coated with a solution of cellulose acetatepthalate being resistant to gastric juice, in a solvent mixture of acetone and isopropanol (equal parts).

Example 9.

Carbamide peroxide	50 g
Sodium thiocyanate	20 g
Lactoperoxidase (50 U/mg)	1 g
Lactose	100 g
Stearic acid powder	2 g

The carbamide peroxide is granulated using a solution of "Eudragit" S. The lactoperoxidase is mixed with lactose and thiocyanate, and the mixture is granulated using "Eudragit" S. The two batches of granules are combined and mixed with stearic acid powder and the final mixture is tabletted. The tablets have an average weight of about 175 mg.

Example 10.

I	Sodium percarbonate	100 g
	Mannitol	20 g
II	Sodium thiocyanate	40 g
	Mannitol	20 g
III	Lactoperoxidase	2 g
	Mannitol	20 g

Granulates were prepared from each of I, II, and III using a solution of "Eudragit" L. The granules combined were mixed with a suitable flavoring agent as sugar, cocoa, microencapsulated citrus aroma, or mixtures thereof.

A dosage device, e.g. a spoon, which provides for a dose of about 200 mg is enclosed with the package of the granular mixture. The package is made of a moist-tight material e.g. a laminated aluminium foil.

Biological effect

4 test tubes containing 10 mls of whey

having a content of 21 ppm (0.25 mM) of NaSCN were incubated at 30°C, the whey having been inoculated with *Ps. fluorescens* EF 1998. One tube was control. Sodium percarbonate corresponding to 0.1 mM, 02 mM, and 0.3 mM, respectively, of H_2O_2 was added respectively to the three other tubes. The amounts of bacteria was determined at inoculation and after 2 hrs of incubation. Lactoperoxidase is present in an amount of 5 μg/ml. The result is given in Table 1 below.

TABLE 1

Na-percarbonate corresponding to mM H_2O_2	Number of bacteria/ml	
	0 hr	2 hrs
Control (0.0 mM)	$2.1 \cdot 10^6$	$2.1 \cdot 10^6$
0.1 mM	$2.1 \cdot 10^6$	$1.8 \cdot 10^5$
0.2 mM	$2.1 \cdot 10^6$	$2.8 \cdot 10^3$
0.3 mM	$2.1 \cdot 10^6$	$2.6 \cdot 10^3$

As is evident from Table 1, a striking improvement in the antibacterial effect is obtained when 0.2 mM H_2O_2 or more are present. However, even the addition of 0.1 mM H_2O_2 gives a noticeable bactericidal effect.

Ps. fluorescens EF 1998 was incubated at +30°C in two tubes 1) and 2). Tube 1) contained 1 g of a commercial milk replacer comprising 15% of ultrafiltrated whey powder, 57% of whey powder, 8% of fat, 16% of animalic protein and 4% of vitamins and minerals in 10 mls of water, whereby it contained 50 μg of lactoperoxidase, and 27.5 ppm of sodium percarbonate were added thereto, and tube 2) contained the same amount of milk replacer (50 μg of lactoperoxidase) and 21 ppm of sodium thiocyanate and 27.5 ppm of sodium percarbonate were added thereto.

The amount of bacteria in the different tubes is given in Table 2 below, where the result after 0, 2, 4 and 6 hrs is given.

TABLE 2

Sample	0	2	4	6 hrs
Tube 1	$4.5 \cdot 10^6$	$3.5 \cdot 10^6$	$5.3 \cdot 10^6$	$6.0 \cdot 10^6$
Tube 2	$4.5 \cdot 10^6$	$3.5 \cdot 10^5$	$5.3 \cdot 10^4$	$5.6 \cdot 10^3$

As is evident from Table 2 the amount of bacteria in tube 2) after 6 hrs is only 1/1000 of the amount in tube 1) at the same time. No or only slight growth has taken place in tube 1) but the bacteria have been killed in tube 2).

The effect of the antibacterial system was determined in vitro. Different *E. coli* strains were incubated at +37°C in an aqueous solution of 5 g of whey-powder/100 ml, 21 ppm of NaSCN and sodium percarbonate corresponding to 0.25 mM H_2O_2. The result of the *E. coli*-killing after 2 hrs is given in Table 3 below.

TABLE 3

E. coli strain		% killed
0–139	299/66	>99.98
0–149	853/67	>99.98
0–138	355/67	>99.95
0–8	915/66	>99.99
0–147	949/66	>99.99
0–141	220/65	>99.99

Several of the *E. coli* strains tested above are resistant to antibiotics. Thus the results indicate a high degree of application of the system.

A high degree of application is also present as the system has an effect on gram positive bacterias, too.

The antibacterial system according to the invention may also be utilized in foodstuffs for human use as well as in pharmaceutical preparation for veterinarian and human use. As pharmaceutical preparations solid as well as liquid preparations may be used; the antibacterial system is generally added to pharmaceutical carriers of different kinds, depending on type and amount used.

A milk substitute intended for calves and containing 45% by weight of skim milk powder (⩾40 mg LP/kg), 22.5% by weight of whey powder, 12.5% by weight of soya meal, 15.0% by weight of animal fat, 4.5% by weight of lactalbumins and 0.5% by weight of vitamins was used in a test against *E. coli* 9703. The strain was incubated at +37°C in a 10% aqueous solution of the milk replacer containing 5 μg/ml of lactoperoxidase. Two different concentrations of NaSCN and three different concentrations of H_2O_2 in form of Na-percarbonate were used, as given in Table 4 below.

TABLE 4

Conc. in mM		Number of bacteria/ml	
SCN^-	H_2O_2	at 0 hrs	2 hrs
0.25	0	$2.5 \cdot 10^6$	$7.7 \cdot 10^7$
0.25	0.25	$2.5 \cdot 10^6$	$5.3 \cdot 10^4$
0.50	0	$1.8 \cdot 10^6$	$1.0 \cdot 10^8$
0.50	0.50	$1.8 \cdot 10^6$	$1.5 \cdot 10^4$

As is evident from Table 4, the antibacterial system gives a strong bactericidal effect in both concentrations tested, simultaneously as it is shown that SCN^- has no effect *per se*, and bacterial growth continues when no peroxide donor is present.

WHAT WE CLAIM IS:—

1. A foodstuff or animal feedstuff comprising an antibacterial system which is activated in the gastrointestinal tract, and comprises a lactoperoxidase, a thiocyanate and a solid, water soluble peroxide donor which is

an alkali metal percarbonate, an alkaline earth metal peroxide, or a carbamide peroxide.

2. Foodstuff or animal feedstuff according to claim 1 which comprises a thiocyanate in an amount of at least 16 ppm of the total composition calculated as NaSCN, the peroxide donor in an amount of at least 21 ppm of the total composition calculated as sodium percarbonate, and a lactoperoxidase in pure form and/or in the from of a lactoperoxidase-containing milk product in an amount of at least 1 mg/kg of the total composition, the molar ratio of peroxide donor to thiocyanate being less than 4:1.

3. A foodstuff or animal feedstuff according to claim 2 wherein the said molar ratio is 1:1 to 2:1.

4. A foodstuff or animal feedstuff according to any one of claims 1 to 3 wherein the thiocyanate is present in an amount of 160 to 3500 ppm calculated as sodium thiocyanate, the peroxide donor is present in an amount of 210 to 4000 ppm calculated as sodium percarbonate, and the lactoperoxidase is present in an amount of 10 to 200 mg/kg.

5. A foodstuff or animal feedstuff according to claim 4 which comprises the thiocyanate in an amount of 160 to 1750 ppm calculated as sodium thiocyanate, the peroxide donor in an amount of 210 to 2000 ppm calculated as sodium percarbonate and the lactoperoxidase in an amount of 10 to 100 mg/kg.

6. A foodstuff or animal feedstuff according to any one of the preceding claims wherein the solid, water soluble peroxide donor is sodium percarbonate.

7. A foodstuff or animal feedstuff according to claim 6 wherein the sodium percarbonate is provided with a protective layer dissolvable in the intestinal tract.

8. A foodstuff or animal feedstuff according to claim 7 wherein the protective layer consists of cellulose acetatephthalate.

9. A foodstuff or animal feedstuff according to claim 1 substantially as hereinbefore described with reference to any one of Examples 1 to 6.

10. A process for the preparation of a foodstuff or animal feedstuff wherein an antibacterial system which is activated in the gastorintestinal tract, is added to a foodstuff or animal feedstuff known *per se*, said system comprising a lactoperoxidase, a thiocyanate, and a solid, water soluble peroxide donor which is an alkali metal percarbonate, alkaline earth metal peroxide, or a carbamide peroxide.

11. A process according to claim 10, wherein the thiocyanate is added in an amount of at least 16 ppm of the total composition calculated as NaSCN, the peroxide donor is added in an amount of at least 21 ppm of the total composition calculated as sodium percarbonate and a lactoperoxidase in pure form and/or in the form of a lactoperoxidase-containing milk product is added in an amount of at least 1 mg/kg of the total composition, the molar ratio of the peroxide donor to thiocyanate being less than 4:1.

12. A process according to claim 11 wherein the said molar ratio is 1:1 to 2:1.

13. A process according to claim 11 or 12 wherein the thiocyanate is added in an amount of 160 to 3500 ppm, calculated as sodium thiocyanate, the peroxide donor is added in an amount of 210 to 4000 ppm calculated as sodium percarbonate, and the lactoperoxidase is added in an amount of 10 to 200 mg/kg.

14. A process according to claim 13 wherein the thiocyanate is added in an amount of 160 to 1750 ppm calculated as sodium thiocyanate, the peroxide donor is added in an amount of 210 to 2000 ppm calculated as sodium percarbonate and the lactoperoxidase is added in an amount of 10 to 100 mg/kg.

15. A process according to any one of claims 10—14 wherein the peroxide donor is sodium percarbonate.

16. A process according to claim 15 wherein the sodium percarbonate is in granular form and coated with a protecting layer, which dissolves and/or becomes permeable in the intestinal tract.

17. A process according to claim 16 wherein the protective layer consists of cellulose acetate-phthalate.

18. A process for the preparation of a foodstuff or animal feedstuff according to claim 10 substantially as hereinbefore described with reference to any one of Examples 1 to 6.

19. A foodstuff or animal feedstuff obtained by a process according to any one of claims 10—18.

20. A method of meat production which comprises feeding a meat producing animal with an animal feedstuff according to any one of claims 1—9 or 19.

21. A method according to claim 20 wherein the thiocyanate is administered in an amount of at least 16 ppm of the feeding stuff calculated as NaSCN and/or in such an amount that the concentration thereof in the intestinal tract is at least 0.1 mM, the peroxide donor is administered in an amount of at least 21 ppm of the feeding stuff calculated as sodium percarbonate and/or in such an amount, calculated as H_2O_2, that the concentration thereof in the intestinal tract is at least 0.1 mM, and lactoperoxidase is administered in an amount of at least 1 mg/kg of feeding stuff and/or in such an amount that the concentration thereof is at least 1 mg/l of intestinal contents.

22. An antibacterial system comprising a lactoperoxidase, thiocyanate, and a solid, water soluble peroxide donor which is an alkali metal percarbonate, an alkaline earth metal peroxide, or a carbamide peroxide.

23. An antibacterial system according to

claim 22 substantially as hereinbefore described with reference to any one of the Examples.

24. A pharmaceutical composition comprising an antibacterial system according to claim 22 or 23 together with a pharmaceutically acceptable carrier.

25. A composition according to claim 24 substantially as hereinbefore described with reference to any one of Examples 7 to 10.

26. A method of treating gastrointestinal infections in mammals excluding humans which comprises administering orally to a mammal suffering from gastrointestinal infection an antibacterial system according to claim 22 or 23 or a composition according to claim 24 or 25.

27. A method of treating topical bacterial infections in mammals excluding humans which comprises administering topically to a mammal suffering from topical bacterial infection an antibacterial system according to claim 22 or 23 or a composition according to claim 24 or 25.

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